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Proposed Registration Document PRD2013-21

Tembotrione

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Overview

Proposed Registration Decision for Tembotrione

Health Canada's Pest Management Regulatory Agency (PMRA), under the authority of the *Pest Control Products Act* and Regulations, is proposing full registration for the sale and use of Tembotrione Technical Herbicide (technical grade active ingredient) and Vios G3 (end-use product), containing the technical grade active ingredients tembotrione and thiencarbazone-methyl, to control annual broadleaved and grassy weeds in field corn.

Tembotrione Technical Herbicide (Registration Number 29657) and Vios G3 (Registration Number 29643) are conditionally registered in Canada. The detailed review for Tembotrione Technical Herbicide and Vios G3 can be found in Evaluation Report ERC2012-02. The current applications were submitted to convert Tembotrione Technical Herbicide and Vios G3 from conditional registration to full registration.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

This Overview describes the key points of the evaluation, while the Science Evaluation provides detailed technical information on the human health, environmental and value assessments of Tembotrione Technical Herbicide and Vios G3.

What Does Health Canada Consider When Making a Registration Decision?

The key objective of the *Pest Control Products Act* is to prevent unacceptable risks to people and the environment from the use of pest control products. Health or environmental risk is considered acceptable[1] if there is reasonable certainty that no harm to human health, future generations or the environment will result from use or exposure to the product under its proposed conditions of registration. The Act also requires that products have value[2] when used according to the label directions. Conditions of registration may include special precautionary measures on the product label to further reduce risk.

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1 "Acceptable risks" as defined by subsection 2(2) of the *Pest Control Products Act*.

2 "Value" as defined by subsection 2(1) of the *Pest Control Products Act*: "the product's actual or potential contribution to pest management, taking into account its conditions or proposed conditions of registration, and includes the product's (*a*) efficacy; (*b*) effect on host organisms in connection with which it is intended to be used; and (*c*) health, safety and environmental benefits and social and economic impact."

To reach its decisions, the PMRA applies modern, rigorous risk-assessment methods and policies. These methods consider the unique characteristics of sensitive subpopulations in humans (for example, children) as well as organisms in the environment (for example, those most sensitive to environmental contaminants). These methods and policies also consider the nature of the effects observed and the uncertainties when predicting the impact of pesticides. For more information on how the PMRA regulates pesticides, the assessment process and risk-reduction programs, please visit the Pesticides and Pest Management portion of Health Canada's website at healthcanada.gc.ca/pmra.

Before making a final registration decision on tembotrione, the PMRA will consider all comments received from the public in response to this consultation document.[3] The PMRA will then publish a Registration Decision[4] on tembotrione, which will include the decision, the reasons for it, a summary of comments received on the proposed final registration decision and the PMRA's response to these comments.

For more details on the information presented in this Overview, please refer to the Science Evaluation of this consultation document.

What Is Tembotrione?

Tembotrione is an active ingredient in the end-use product Vios G3, which is a co-formulation of 350 g/L tembotrione and 70 g/L thiencarbazone-methyl. Vios G3 is a postemergence herbicide for the control of annual broadleaf and grassy weeds in field corn using ground application equipment only.

Tembotrione is a WSSA (Weed Science Society of America) Group 27 herbicide. Tembotrione inhibits the enzyme 4-hydroxyphenyl-pyruvate-dioxygenase (4-HPPD) in target plants. Inhibition of 4-HPPD disturbs chloroplast synthesis and functions. Sensitive plants exhibit symptoms in the form of strong bleaching effects, especially on the actively growing zone of shoots, and then die within two weeks.

Health Considerations

Can Approved Uses of Tembotrione Affect Human Health?

Tembotrione is unlikely to affect your health when used according to label directions.

Potential exposure to tembotrione may occur through the diet (food and water) or when handling and applying the product. When assessing health risks, two key factors are considered: the levels where no health effects occur and the levels to which people may be exposed. The dose levels

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3 "Consultation statement" as required by subsection 28(2) of the *Pest Control Products Act*.

4 "Decision statement" as required by subsection 28(5) of the *Pest Control Products Act*.

used to assess risks are established to protect the most sensitive human population (for example, children and nursing mothers). Only uses for which the exposure is well below levels that cause no effects in animal testing are considered acceptable for registration.

Toxicology studies in laboratory animals describe potential health effects from varying levels of exposure to a chemical and identify the dose where no effects are observed. The health effects noted in animals occur at doses more than 100 times higher (and often much higher) than levels to which humans are normally exposed when tembotrione products are used according to label directions.

The technical grade active ingredient Tembotrione was found to be a potential dermal sensitizer and requires the statement "Potential Skin Sensitizer" on the label.

The end-use product Vios G3 was mildly irritating to the eye. For this reason, the statement "Caution - eye irritant" is required on the label.

Tembotrione was not genotoxic. There was no evidence of carcinogenicity in the mouse. However, in long-term studies, there was evidence that tembotrione caused squamous cell carcinomas in the eye in rats due to long-term effects on that organ. There were indications that tembotrione potentially caused damage to the nervous system in rats and dogs at doses that caused other effects in test animals. The main signs of toxicity in animals given daily doses of tembotrione over longer periods of time were white areas on the eyes and keratitis-related changes to the cornea, mild haemorrhagic changes and liver, kidney and pancreatic changes. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

When tembotrione was given to pregnant animals, effects on the developing fetus were observed at doses that were toxic to the mother. However, since effects in the fetus were of a more severe nature than those seen in the mother, the fetus is considered more sensitive to tembotrione than the adult animal. Because of this observation, extra protective measures were applied during the risk assessment to further reduce the allowable level of human exposure to tembotrione.

Residues in Water and Food

Dietary risks from food and water are not of concern.

Aggregate dietary intake estimates (food plus water) revealed that the general population and children 3–5 years old, the subpopulation which would ingest the most tembotrione relative to body weight, are expected to be exposed to less than 29% of the acceptable daily intake. Based on these estimates, the chronic dietary risk from tembotrione is not of concern for all population subgroups. There were no cancer risks of concern for tembotrione.

Acute dietary (food and water) estimates for the general population and all population subgroups were less than 47% of the acute reference dose, and are not of health concern. The highest exposed subpopulation was infants less than one year old.

The *Food and Drugs Act* prohibits the sale of adulterated food, that is, food containing a pesticide residue that exceeds the established maximum residue limit (MRL). Pesticide MRLs are established for *Food and Drugs Act* purposes through the evaluation of scientific data under the *Pest Control Products Act*. Food containing a pesticide residue that does not exceed the established MRL does not pose an unacceptable health risk.

Residue trials conducted throughout Canada and the United States using tembotrione on corn were acceptable to support the domestic uses. No new MRLs in/on corn are recommended at this time as MRLs for corn (field, sweet and pop) were previously recommended to cover residues in imported commodities. The MRLs for this active ingredient in animal commodities as a result of domestic use on field corn can be found in the Science Evaluation section of ERC2012-02.

Occupational Risks From Handling Vios G3

Occupational risks are not of concern when Vios G3 is used according to the label directions, which include protective measures.

Farmers and custom applicators who mix, load or apply Vios G3, as well as field workers re-entering freshly treated fields, can come in direct contact with tembotrione residues on the skin or through inhalation of spray mists.

Therefore, the label will specify appropriate personal protective equipment such as long-sleeved shirt, long pants, chemical-resistant gloves, socks and shoes, chemical-resistant coveralls, goggles or faceshield, or engineering controls for anyone conducting specific tasks with the end-use product. In addition, restrictions on the amount of product handled per day, and restricted-entry intervals for certain postapplication activities are required. Taking into consideration these label requirements, risks to agriculture workers are not of concern.

For bystanders, exposure is expected to be much less than that of field workers and is considered negligible. Therefore, health risks to bystanders are not of concern.

Environmental Considerations

What Happens When Tembotrione Is Introduced Into the Environment?

Tembotrione is moderately to highly mobile and exhibits variable persistence in laboratory soil. Data specifically designed to investigate the extent of these properties demonstrate that it is not expected to leach significantly under field conditions in Canadian soils. Tembotrione is toxic to small mammals, terrestrial plants, freshwater vascular plants, and estuarine/marine invertebrates. Tembotrione poses a negligible risk to earthworms, honey bees, birds, freshwater invertebrates, freshwater and marine fish, and freshwater and marine algae.

In soil, tembotrione is expected to break down in the presence of oxygen; however, in soils lacking oxygen, tembotrione is expected to persist. New information allowed for the calculation

of revised half-lives and characterization of important breakdown products. Despite the relatively shorter half-lives in soil, it is still evident that tembotrione behaves quite differently depending on the soil type.

Tembotrione very easily dissolves in water. When it enters the aquatic environment, it tends to settle out of the water column and ends up in the sand or sediment. Tembotrione can persist in certain aquatic environments.

New laboratory studies indicate that tembotrione is expected to move downward through the soil, confirming previous data indicating high soil mobility. However, three additional lysimeter studies (two in Ontario and one in Quebec) showed that tembotrione did not leach significantly under Canadian field conditions. In terrestrial field studies tembotrione dissipated rapidly and did not appear to travel very deeply into the soil.

Tembotrione is not likely to breakdown by reacting with water or sunlight. Tembotrione is also unlikely to enter the atmosphere and travel long distances in air. Residues of tembotrione are unlikely to accumulate in organisms.

Tembotrione has several different breakdown products, some of which have the potential to move down through the soil, however they breakdown fairly rapidly.

Non-target organisms that may be vulnerable to adverse effects resulting from potential tembotrione exposure include terrestrial plants, freshwater aquatic plants, estuarine/marine invertebrates, and small mammals.

Value Considerations

What is the Value of Vios G3?

Vios G3, a postemergence herbicide, is for selective control of annual broadleaved and grassy weeds in field corn using ground application equipment only.

Vios G3 at a rate of 110 mL/ha (i.e. 38.5 g a.i./ha tembotrione + 7.7 g a.i./ha thiencarbazone-methyl) is labelled for application in tank mix with Liberty herbicide (i.e. glufosinate ammonium) or glyphosate herbicide on Liberty Link (i.e. glufosinate ammonium resistant varieties) or glyphosate tolerant field corn, respectively. The tank mixes must be applied postemergence to field corn at the one- to six-leaf stage.

A single application of Vios G3 in these tank mixes provides residual control of numerous annual broadleaved and grassy weeds, including Group 2 herbicide resistant biotypes. Application of Vios G3 is compatible with integrated weed management practices and with conservation tillage and conventional crop production systems. Vios G3 is a postemergence herbicide applied after weeds have emerged. Growers can therefore better assess whether the herbicide is necessary or suitable for particular weed species. In addition, Vios G3, containing the Group 27 herbicide component tembotrione, provides Canadian corn growers with an

alternative weed management tool to control weeds that have developed resistance to other herbicide modes of action.

Vios G3 also contains thiencarbazone-methyl, a WSSA Group 2 herbicide, which inhibits the enzyme acetolactate synthase (ALS) in target plants. Inhibition of ALS starves the plants of essential amino acids and leading plants to chlorosis and necrosis and eventually to death.

Measures to Minimize Risk

Labels of registered pesticide products include specific instructions for use. Directions include risk-reduction measures to protect human and environmental health. These directions must be followed by law.

The key risk-reduction measures on the label of Vios G3 to address the potential risks identified in this assessment are as follows.

Key Risk-Reduction Measures

Human Health

Because there is a concern with farmers, custom applicators, or field workers re-entering freshly treated fields coming into direct contact with Vios G3 on the skin or through inhalation of spray mists, anyone mixing, loading and applying Vios G3 must wear appropriate personal protective equipment.

The Vios G3 label specifies that anyone mixing, loading or applying the product must wear chemical-resistant coveralls and shoes plus socks. Workers mixing or loading Vios G3 must also wear chemical-resistant gloves and protective eyewear. Workers must not apply Vios G3 to more than 150 hectares per day. The Vios G3 label requires that workers do not enter treated fields for 12 hours after application.

In addition, standard label statements to protect against drift during application were added to the product label.

Environment

Due to the risks identified for tembotrione, specific mitigation measures are necessary to protect the environment. In order to protect terrestrial and nearby freshwater and estuarine/marine habitats, both aquatic spray buffer zones (1 m) and terrestrial spray buffer zones (10 m) have been determined to be necessary for tembotrione-containing end-use products. If tembotrione is applied in combination with other pesticides, the most restrictive spray buffer zones must be observed. Toxicity label statements are required for sensitive organisms including non-target plants, aquatic invertebrates, and small mammals.

Next Steps

Before making a final registration decision on tembotrione, the PMRA will consider all comments received from the public in response to this consultation document. The PMRA will accept written comments on this proposal up to 45 days from the date of publication of this document.

Please forward all comments to Publications (contact information on the cover page of this document). The PMRA will then publish a Registration Decision, which will include its decision, the reasons for it, a summary of comments received on the proposed final decision and the Agency's response to these comments.

Other Information

When the PMRA makes its registration decision, it will publish a Registration Decision on tembotrione (based on the Science Evaluation of this consultation document). In addition, the test data referenced in this consultation document will be available for public inspection, upon application, in the PMRA's Reading Room (located in Ottawa).

Science Evaluation

Tembotrione

1.0 The Active Ingredient, Its Properties and Uses

Vios G3 is formulated as a suspension containing tembotrione at 350 g/L and thiencarbazone-methyl at 70 g/L. This end-use product has a density of 1.2347 g/mL and pH of 3.16 (10% solution). The chemistry requirements for Vios G3 have been fulfilled.

1.1 Identity of the Active Ingredient

Please refer to Evaluation Report ERC2012-02, *Tembotrione*, for details.

1.2 Physical and Chemical Properties of the Active Ingredient and End-use Product

Please refer to Evaluation Report ERC2012-02.

1.3 Directions for Use

Vios G3, containing 350 g/L tembotrione and 70 g/L thiencarbazone-methyl, is a selective herbicide for use as a postemergence treatment in tank mix with Liberty herbicide (i.e. glufosinate ammonium) or glyphosate herbicide on Liberty Link (i.e. glufosinate ammonium resistant varieties) or glyphosate tolerant field corn, in Eastern Canada only. The product is applied once per growing season, to field corn at the one- to six-leaf stage, at a rate of 110 mL/ha (Table 1.3.1) with ground application equipment only.

Table 1.3.1 Efficacy claims for Vios G3

Products	Rates	For residual control of following weeds
Vios G3 + Liberty 200 SN Herbicide	110 mL/ha 2.0–2.5 L/ha	lamb's-quarters, redroot pigweed, wild buckwheat, lady's thumb, wild mustard, common hempnettle, common chickweed, spiny annual sowthistle, common ragweed, velvetleaf, Eastern black nightshade, green foxtail, yellow foxtail, barnyard grass, witchgrass, and large crabgrass
Vios G3 + glyphosate	110 mL/ha 900 g a.e./ha	

1.4 Mode of Action

Tembotrione is a WSSA Group 27 herbicide. The primary mode of action of tembotrione is as an inhibitor of 4-hydroxyphenylpyruvate dioxygenase (4-HPPD) in the biosynthesis of plastoquinones, tocopherols and carotenoids. Blockage of the pathway at this enzymatic site

leads to disturbed chloroplast synthesis and function as well as to photobleaching by oxidative degradation of chlorophyll and destruction of the photosynthetic membranes. Sensitive weed species exhibit symptoms within 2–5 days in the form of strong bleaching effects, particularly on the growing zones of shoots. After treatment, growth is inhibited, chlorotic tissues become necrotic under the influence of light, and sensitive plants typically die within 14 days.

2.0 Methods of Analysis

Please refer to Evaluation Report ERC2012-02 for more details on Methods for Analysis of the Active Ingredient, Method for Formulation Analysis, and Methods for Residue Analysis.

3.0 Impact on Human and Animal Health

3.1 Toxicology Summary

A detailed review of the toxicological database for tembotrione was conducted. The database is complete, consisting of the full array of toxicity studies currently required for hazard assessment purposes. The studies were carried out in accordance with currently accepted international testing protocols and Good Laboratory Practices. The scientific quality of the data is high and the database is considered adequate to define the majority of the toxic effects that may result from exposure to this chemical pest control product.

Please refer to Evaluation Report ERC2012-02 for more details on Acute Reference Dose, Acceptable Daily Intake and the Occupational and Residential Risk Assessment.

3.2 Food Residues Exposure Assessment

3.2.1 Residues in Plant and Animal Foodstuffs

Please refer to Evaluation Report ERC2012-02 for a summary of the previously reviewed data and the rationale for the regulatory decision. The information captured herein only relates to the data regarding characterization of the movement of tembotrione in soil provided to the Agency in support of the conversion from conditional to full registration, and the change in the chronic and acute dietary exposure results due to the modification of the estimated environmental concentration values of tembotrione in drinking water.

3.2.2 Dietary Risk Assessment

Acute and chronic dietary risk assessments were conducted using the Dietary Exposure Evaluation Model (DEEM–FCID™, Version 2.14), which uses updated food consumption data from the United States Department of Agriculture's Continuing Surveys of Food Intakes by Individuals, 1994–1996 and 1998.

3.2.2.1 Chronic Dietary Exposure Results and Characterization

The following criteria were applied to the refined chronic analysis: 100% crop treated, supervised trial median residue values for corn commodities, default and experimental processing factors where available, and anticipated residue values in animal commodities. Aggregate exposure from food and water is considered acceptable for the total population, including infants and children, and all representative population subgroups. The PMRA estimates that the refined chronic dietary exposure to tembotrione from all supported tembotrione food uses and water is 12.6% of the ADI for the total population (0.000050 mg/kg bw/day). The highest exposure and risk estimate is for children 3–5 years old at 28.3% of the ADI (0.000113 mg/kg bw/day).

3.2.2.2 Acute Dietary Exposure Results and Characterization

The following criteria were applied to the refined acute analysis: 100% crop treated, the highest average residue values from field corn and popcorn trials and the highest residue value from sweet corn field trials, default and experimental processing factors where available, and anticipated residue values in animal commodities. Aggregate exposure from food and water is considered acceptable for the total population, including infants and children, and all representative population subgroups. The refined aggregate acute dietary exposure (food and water) for all supported tembotrione registered commodities is estimated to be 21.6% (0.000173 mg/kg/day) of the ARfD (95th percentile, deterministic) for the total population. The highest exposure and risk estimate is for infants less than one year old at 46.4% (0.000371 mg/kg bw/day) of the ARfD.

3.2.3 Aggregate Exposure and Risk

The aggregate risk for tembotrione consists of exposure from food and drinking water sources only; there are no residential uses.

3.2.4 Maximum Residue Limits

Please refer to Evaluation Report ERC2012-02 for the proposed MRLs for tembotrione as well as the nature of the residues in animal and plant matrices, analytical methodology and field trial data. The acute and chronic dietary risk estimates are summarized in Appendix I, Table 1.

4.0 Impact on the Environment

The fate and environmental behaviour of tembotrione, as well as its impacts on non-target terrestrial and aquatic organisms, have been previously assessed (for details see Evaluation Report ERC2012-02). The environmental fate data required as a condition of registration (outdoor lysimeter studies conducted on Canadian soils) have been submitted and reviewed. These data satisfy the environmental assessment requirements for foliar use of tembotrione on outdoor agricultural crops.

4.1 Fate and Behaviour in the Environment

Additional fate data were provided, subsequent to the original review, and the following is a summary of the evaluation of these studies.

A laboratory study of biotransformation in aerobic soil showed significantly shorter DT_{50} values in aerobic soil (12.9 to 35.9 days at 20°C) compared to estimates from previously submitted data. The 80th percentile of all aerobic soil biotransformation DT_{50} values (including newly submitted data combined with previously submitted data) resulted in a revised aerobic soil dissipation half-life of 89 days.

Laboratory studies of adsorption resulted in low soil adsorption coefficient values which range from 99 to 227 L/kg. Although the values are higher than previously reported (23.0 L/kg to 92.7 L/kg), they are still within the range that indicates that tembotrione is expected to have moderately high to high mobility in soils.

In order to investigate the leaching potential of tembotrione, a specialized field lysimeter study was conducted under controlled field conditions. The study used replicated 24 cm × 96 cm columns from three coarse-textured soils, two from Ontario and one from Quebec and an application rate of 64 g tembotrione/ha. Measured bromide concentrations (applied as KBr) showed partial to near complete breakthrough indicating adequate methodology for the measurement of leachate concentrations. Tembotrione was not detected in either the leachate from the columns, or within the columns when they were sectioned. The results indicate that the parent compound, tembotrione, did not leach significantly under specific field conditions tested.

A summary of the terrestrial environmental fate and behavior of tembotrione derived from the new study data can be found in Appendix 1, Table 2.

4.2 Environmental Risk Characterization

A comprehensive environmental risk assessment for the foliar use of tembotrione on non-target terrestrial and aquatic organisms has previously been conducted (Evaluation Report ERC2012-02). The results of the original assessment indicated that the risks to the environment are acceptable when the product is used according to label instructions. The currently proposed use rate and the already registered use rate and pattern are identical. Therefore, no further risk to the environment is expected.

5.0 Value

Please refer to Evaluation Report ERC2012-02 for a detailed evaluation of the value of Vios G3.

The outstanding information identified as a condition of registration included establishing the value of the tembotrione component of Vios G3 at the rate of 38.5 g a.i./ha.

Value information submitted, including efficacy data from 14 trials, use history information, and a rationale, confirms that the tembotrione component of Vios G3 at 38.5 g a.i./ha provides control of those listed weeds, for which Group 2 herbicide resistant biotypes have been confirmed, that may not be controlled by the thiencarbazone-methyl component.

The condition of registration for value has been satisfied through the submission of trial data, use history information, and a scientific rationale.

6.0 Pest Control Product Policy Considerations

Please refer to Evaluation Report ERC2012-02 for details on Toxic Substances Management Policy Considerations and Formulants and Contaminants of Health or Environmental Concern.

7.0 Summary

7.1 Human Health and Safety

The toxicology database submitted for tembotrione is adequate to define the majority of potential toxic effects that may result from exposure to tembotrione. In subchronic and chronic studies on laboratory animals, the primary targets were the eye, liver, kidney, pancreas, thyroid, gallbladder and bone marrow. There was evidence of carcinogenicity of the rat in the eye, but only at doses where distinct eye changes were previously noted. There was evidence of increased sensitivity of the young in reproduction and developmental neurotoxicity studies. Tembotrione is a potential neurotoxicant based on peripheral nerve damage in dogs, lack of habituation in the subchronic neurotoxicity study in male rats and brain morphometric changes in the developmental neurotoxicity study. The risk assessment protects against these effects by ensuring that the level of human exposure is well below the lowest dose at which these effects occurred in animal tests.

The nature of the residue in corn and animals is adequately understood. The residue definition is tembotrione and M5. The use of tembotrione on field corn will not constitute an unacceptable chronic or acute dietary risk (food and drinking water) to any segment of the population, including infants, children, adults and seniors. Sufficient crop residue data have been reviewed to recommend maximum residue limits. Please refer to Evaluation Report ERC2012-02 for more details.

Mixers, loaders, and applicators handling Vios G3 and workers re-entering treated corn fields in Eastern Canada are not expected to be exposed to levels of tembotrione and thiencarbazone-methyl that will result in an unacceptable risk when Vios G3 is used according to label directions. The personal protective equipment, restricted-entry intervals, and other mitigation measures on the product label are adequate to protect workers when Vios G3 is used according to label directions.

7.2 Environmental Risk

As indicated in the original environmental assessment (Evaluation Report ERC2012-02), tembotrione poses a negligible risk to earthworms, honey bees, birds, freshwater invertebrates, freshwater and marine fish, and freshwater and marine algae. However, it is above the level of concern for small mammals, terrestrial plants, freshwater vascular plants, and marine/estuarine invertebrates. Thus, toxicity label statements, and spray buffer zones are required for any tembotrione-containing end-use products. Tembotrione is highly mobile and exhibits variable persistence in soil. Additional data submitted to investigate the risk of reaching groundwater demonstrate that tembotrione is not expected to leach significantly under Canadian field soil conditions.

Previously identified data gaps for tembotrione included the need to further characterize the risk of leaching to groundwater (Evaluation Report ERC 2012-02). The required data were derived from three outdoor lysimeter studies which were conducted in Canada on soils with a pH range of 5.8–7 (pH measured in water). These data were submitted in the support of the current registration and were found to be acceptable. Thus, there are no further environmental data requirements for tembotrione at this time.

7.3 Value

The value information submitted in support of Vios G3 is adequate to describe its value for use in tank mix combination with Liberty herbicide (i.e. glufosinate ammonium) or glyphosate herbicide on Liberty Link (i.e. glufosinate ammonium resistant varieties) or glyphosate tolerant field corn, respectively. A single postemergence application of Vios G3 at 110 mL/ha in tank mix with Liberty or glyphosate herbicide provides residual control of lamb's-quarters, redroot pigweed, wild buckwheat, lady's thumb, wild mustard, common hempnettle, common chickweed, spiny annual sowthistle, common ragweed, velvetleaf, eastern black nightshade, green foxtail, yellow foxtail, barnyard grass, witchgrass, and large crabgrass.
The submitted phytotoxicity and yield data demonstrate an adequate margin of safety of field corn to Vios G3. Vios G3, containing two active ingredients, one of which is a WSSA Group 27 herbicide, provides residual control of weeds that have developed resistance to WSSA Group 2 herbicide.

8.0 Proposed Regulatory Decision

Health Canada's PMRA, under the authority of the *Pest Control Products Act* and Regulations is proposing full registration for the sale and use of Tembotrione Technical Herbicide and Vios G3, containing the technical grade active ingredients tembotrione and thiencarbazone-methyl, to control annual broadleaved and grassy weeds in field corn.

An evaluation of available scientific information found that, under the approved conditions of use, the product has value and does not present an unacceptable risk to human health or the environment.

List of Abbreviations

4-HPPD	4-hydroxyphenyl-pyruvate-dioxygenase
µg	micrograms
a.e.	acid equivalent
a.i.	active ingredient
ADI	acceptable daily intake
AR	applied radioactivity
ARfD	acute reference dose
ATPD	amount treated per day
bw	body weight
cm	centimetres
DEEM	Dietary Exposure Evaluation Model
DT_{50}	dissipation time 50% (the dose required to observe a 50% decline in concentration)
ERC	Evaluation Report
FDA	Food and Drugs Act
g	gram
ha	hectare(s)
HDPE	high density polyethylene
IUPAC	International Union of Pure and Applied Chemistry
KBr	Potassium Bromide
kg	kilogram
K_{oc}	organic-carbon partition coefficient
K_{ow}	*n*–octanol-water partition coefficient
L	litre
m	metre
m^3	cubic metre
mg	milligram
mL	millilitre
MRL	maximum residue limit
PCPA	Pest Control Products Act
pH	measure of the acidity or basicity of an aqueous solution
p*K*a	dissociation constant
PMRA	Pest Management Regulatory Agency
ppm	parts per million
TGAI	technical grade active ingredient
WSSA	Weed Science Society of America

Appendix I Tables

Table 1 Food Residue Chemistry Overview of Metabolism Studies and Risk Assessment

DIETARY RISK FROM FOOD AND WATER			
	POPULATION	ESTIMATED RISK % of ACCEPTABLE DAILY INTAKE (ADI)	
		Food Only	Food and Water
Refined chronic non-cancer dietary risk ADI = 0.0004 mg/kg bw/day Estimated chronic drinking water concentration = 0.33 μg a.i./L	All infants < 1 year	13.3	19.0
	Children 1–2 years	23.1	25.7
	Children 3–5 years	25.9	28.3
	Children 6–12 years	19.5	21.2
	Youth 13–19 years	14.6	15.9
	Adults 20–49 years	8.8	10.4
	Adults 50+ years	5.1	6.8
	Females 13–49 years	8.7	10.4
	Total population	10.8	12.6
	POPULATION	ESTIMATED RISK % of ACUTE REFERENCE DOSE (ARfD)	
		Food Only	Food and Water
Refined acute dietary exposure analysis, 95th percentile ARfD = 0.0008 mg/kg bw Estimated acute drinking water concentration = 0.37 μg a.i./L	All infants < 1 year	43.0	46.4
	Children 1–2 years	38.5	39.9
	Children 3–5 years	38.3	39.9
	Children 6–12 years	29.0	30.4
	Youth 13–19 years	23.3	24.1
	Adults 20–49 years	15.2	15.9
	Adults 50+ years	9.7	10.7
	Females 13–49 years	15.9	16.6
	Total population	20.7	21.6

Table 2 Fate and Behaviour in the Terrestrial Environment – New Study Data (Additional to ERC 2012-02)[1]

Property	Test substance	Value	Comments
Biotransformation			
Biotransformation in aerobic soil	**TGAI:** tembotrione	**New data at 20°C** DT_{50}: 12.9 days (loam) 22.1 days (sandy loam) 35.9 days (sand) Major Transformation Product: AE 0172747-benzoic acid (AE0456148, previously labelled as M6) Minor Transformation Products: Several unknowns, all less than 5.8% A.R. 80th percentile of new and old data combined – DT_{50}: 89 days	Non-persistent to slightly persistent Moderately persistent
Mobility			
Adsorption	**TGAI:** tembotrione	**New data at 20°C** K_{oc}: 99 (loam) 227 (sandy loam) 126 (sand)	Moderate to high mobility expected
Field Lysimeter	**TGAI:** tembotrione	Tembotrione not detected in leachate.	Tembotrione is not expected to leach significantly under field conditions

K_{oc} = organic-carbon partition coefficient

[1] For comprehensive summary tables of the environmental fate and behaviour properties of tembotrione previously reviewed, see Tables 11 and 12 in Appendix I of ERC 2012-02.

References

A. List of Studies/Information Submitted by Registrant

1.0 Chemistry

PMRA Document Number	Reference
1672976	2008, Storage Stability and Corrosion Characteristics of Thiencarbazone-Methyl +Tembotrione + Isoxadifen-Ethyl SC, DACO: 3.5.10,3.5.14 CBI

2.0 Human and Animal Health

None

3.0 Environment

PMRA Document Number	Reference
2178961	2011, [Phenyl-UL-14C]AE 0172747: Aerobic Degradation Rate in Three Canadian Soils, DACO: 8.2.3.4,8.2.3.4.2
2178962	2011, Adsorption Properties of [14C]-Tembotrione in Three Soils, DACO: 8.2.4.2
2249094	2012, Leaching investigation of tembotrione using field lysimeters in Ontario and Quebec Canada, DACO: 8.3.4
2249095	2012, Leaching investigation of tembotrione using field lysimeters in Ontario and Quebec Canada, DACO: 8.3.4

4.0 Values

PMRA Document Number	Reference
2229133	2012, SC547 Herbicide - Additional information required to fulfill the terms and conditions for conditional registration, DACO 10.1,10.2,10.2.3,10.2.3.1,10.2.3.3,10.2.3.3(B), 147 pages